

Inhibin is more specific than calretinin as an immunohistochemical marker for differentiating sarcomatoid granulosa cell tumour of the ovary from other spindle cell neoplasms.

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ABSTRACT: Aims: To describe a case of recurrent sarcomatoid adult granulosa cell tumour (AGCT) of the ovary and to evaluate the usefulness of two ovarian sex cord stromal markers (inhibin and calretinin) in separating sarcomatoid AGCT from true sarcomas. Methods: A 72 year old woman presented with a recurrent sarcomatoid AGCT in the sigmoid colon mesentery, which histologically mimicked a malignant

\*\*\*gastrointestinal\*\*\* stromal tumour (GIST). This index case and 79 sarcomas (32 GISTs, 28 leiomyosarcomas, 15 endometrial stromal sarcomas (ESSs), including one with sex cord-like areas, and four undifferentiated uterine sarcomas) were immunostained using antibodies to inhibin and calretinin. Results: The recurrent sarcomatoid AGCT expressed diffuse, strong cytoplasmic immunoreactivity with inhibin and focal but strong nuclear and cytoplasmic positivity with calretinin. Focal, weak cytoplasmic inhibin expression limited to sex cord-like areas was present in one ESS. None of the other sarcomas expressed

\*\*\*inhibin\*\*\*. Focal, strong calretinin immunoreactivity was identified in 11 leiomyosarcomas and one GIST. The case of ESS with sex cord-like areas showed strong immunoreactivity for calretinin limited to the sex cord-like areas. Conclusions: \*\*\*Inhibin\*\*\* is a useful immunomarker to distinguish sarcomatoid AGCT from other spindle cell neoplasms that may enter into the differential diagnosis. Calretinin appears to be less specific than \*\*\*inhibin\*\*\*.

? ds

Set	Items	Description
S1	17418	INHIBIN
S2	847892	INTRACELLULAR OR CYTOPLASM
S3	582	S1 AND S2
S4	14830	ACTIVIN
S5	231	S3 AND S4
S6	159	RD (unique items)
S7	761320	COLON OR COLORECTAL OR GASTROINTESTIN?
S8	2	S6 AND S7

? s s3 and s7

	582	S3
	761320	S7
S9	14	S3 AND S7

? rd

S10	12	RD (unique items)
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? t s10/3,k,ab/1-12

10/3,K,AB/1 (Item 1 from file: 155)  
DIALOG(R)File 155:MEDLINE(R)  
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15975754 PMID: 16487364

Activin-A as an intraovarian modulator: actions, localization, and regulation of the intact dimer in human ovarian cells.

Rabinovici J; Spencer S J; Doldi N; Goldsmith P C; Schwall R; Jaffe R B  
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Journal of clinical investigation (UNITED STATES) May 1992, 89 (5)  
p1528-36, ISSN 0021-9738--Print Journal Code: 7802877

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TW; FIC; +

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P.H.S.

Languages: ENGLISH

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The actions, localization, and regulation of activin in the human ovary are unknown. Therefore, the aims of this study were (a) to define the effects of recombinant activin-A and its structural homologue, inhibin-A, on mitogenesis and steroidogenesis (progesterone secretion and aromatase activity) in human preovulatory follicular cells; (b) to localize the activin-A dimer in the human ovary by immunohistochemistry; and (c) to examine regulation of intracellular activin-A production in cultured human follicular cells. In addition to stimulating mitogenic activity, activin-A causes a dose- and time-dependent inhibition of basal and gonadotropin-stimulated progesterone secretion and aromatase activity in human luteinizing follicular cells on day 2 and day 4 of culture. Inhibin-A exerts no effects on mitogenesis, basal or gonadotropin-stimulated progesterone secretion and aromatase activity, and does not alter effects observed with activin-A alone. Immunostaining for dimeric activin-A occurs in granulosa and cumulus cells of human ovarian follicles and in granulosa-lutein cells of the human corpus luteum. cAMP, and to a lesser degree human chorionic gonadotropin and follicle-stimulating hormone, but not inhibin-A, activin-A, or phorbol 12-myristate 13-acetate, increased the immunostaining for activin-A in cultured granulosa cells. These results indicate that activin-A may function as an autocrine or paracrine regulator of follicular function in the human ovary.

...activin-A dimer in the human ovary by immunohistochemistry; and (c) to examine regulation of intracellular activin-A production in cultured human follicular cells. In addition to stimulating mitogenic activity, activin-A causes...

2/3,K,AB/12 (Item 12 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

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08158075 PMID: 2546739

Stimulation of glucose production by activin-A in isolated rat hepatocytes.

Mine T; Kojima I; Ogata E

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Endocrinology (UNITED STATES) Aug 1989, 125 (2) p586-91, ISSN  
0013-7227--Print Journal Code: 0375040

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Document type: Journal Article; Research Support, Non-U.S. Gov't

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

The effect of activin-A on glycogenolysis was studied in isolated rat hepatocytes. Activin-A stimulated glucose output in hepatocytes in a dose-dependent manner. The maximal effect of the glycogenolytic action of

activin-A, which was about 50% of the glucagon action, was obtained at  $10(-9)$  M. When  $10(-9)$  M activin-A and  $5 \times 10(-9)$  M glucagon were added simultaneously, the actions of these two agents were additive. In contrast, there was no additivity when  $10(-9)$  M activin-A and  $10(-8)$  M angiotensin-II were added. Activin-A did not increase cAMP at any doses tested, but induced a rapid increase in cytoplasmic free calcium concentration. Activin-A increased the cytoplasmic free calcium concentration even in the presence of 1 microM extracellular calcium, suggesting that activin-

\*\*\*A\*\*\* caused calcium release from an \*\*\*intracellular\*\*\* calcium pool(s). The internal calcium pool affected by activin-A appeared to be the same as that affected by either angiotensin-II or vasopressin. When [3H] inositol-labeled hepatocytes were incubated with activin-A, radioactivity in the inositol trisphosphate fraction was rapidly increased. These results indicate that activin-A acts on rat hepatocytes and stimulates glycogenolysis by activating the calcium messenger s

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Transforming growth factor-beta 1 and activin A generate anti proliferative signaling in thyroid cancer cells

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ABSTRACT: Transforming growth factor-beta 1 (TGF-beta 1) and activin A (ActA) induce similar intracellular signaling mediated by the mothers' against decapentaplegic homolog (SMAD) proteins. TGF-beta 1 is a potent antimitogenic factor for thyroid follicular cells, while the role of ActA is not clear. In our study, the proliferation of TPC-1, the papillary thyroid carcinoma cell line, was reduced by both recombinant ActA and TGF-beta 1. Due to the concomitant expression of TGF-beta 1 and ActA in thyroid tumors, we investigated the effects of either TGF-beta 1 or ActA gene silencing by RNA interference in TPC-1 cells in order to distinguish the specific participation of each in proliferation and \*\*\*intracellular\*\*\* signaling. An increased proliferation and reduced SMAD2, SMAD3, and SMAD4 mRNA expression were observed in both TGF-beta 1 and ActA knockdown cells. Recombinant TGF-beta 1 and ActA increased the expression of inhibitory SMAD7, whereas they reduced c-MYC. Accordingly, we detected a reduction in SMAD7 expression in knockdown cells while, unexpectedly, c-MYC was reduced. Our data indicate that both TGF-beta 1 and ActA generate SMADs signaling with each regulating the expression of their target genes, SMAD7 and c-MYC. Furthermore, TGF-beta 1 and ActA have an antiproliferative effect on thyroid papillary carcinoma cell, exerting an important role in the control of thyroid tumorigenesis.

Transforming growth factor-beta 1 and activin A generate anti proliferative signaling in thyroid cancer cells

Set	Items	Description
S1	34	(ACTIVIN(W)A) (5N) INTRACELLULAR
S2	19	RD (unique items)
? s activin(w)a		
Processing		
Processing		
Processing		
	15150	ACTIVIN
	33388682	A
S3	4835	ACTIVIN(W)A
? s intracellular		
S4	675066	INTRACELLULAR
? s s3 and s4		
	4835	S3
	675066	S4
S5	225	S3 AND S4
? s colon		
S6	287992	COLON
? s s5 and s6		
	225	S5
	287992	S6
S7	0	S5 AND S6
? s cancer		
S8	1895473	CANCER
? s s5 and s8		
	225	S5
	1895473	S8
S9	21	S5 AND S8

12039902    Genuine Article#: 723JP    Number of References: 38

Title: Activin beta(C)-subunit heterodimers provide a new mechanism of regulating activin levels in the prostate (ABSTRACT AVAILABLE)

Author(s): Mellor SL; Ball EMA; O'Connor AE; Ethier JF; Cranfield M; Schmitt JF; Phillips DJ; Groome NP; Risbridger GP (REPRINT)

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Abstract: Activins are formed by dimerization of beta-subunits and, as members of the TGF-beta superfamily, have diverse roles as potent growth and differentiation factors. As the biological function of the activin C homodimer (beta(C)-beta(C)) is unknown, we sought to compare activin A (beta(A)-beta(A)), B (beta(B)-beta(B)), and C homodimer bioactivities and to investigate the consequences of activin beta(C)-subunit overexpression in prostate tumor cells. Exogenous activin A and B homodimers inhibited cell growth and activated activin-responsive promoters. In contrast, the activin C homodimer was unable to elicit these responses. We previously showed that the activin beta(C)-subunit heterodimerized with activin beta(A) in vitro to form activin AC. Therefore, we hypothesize that the activin beta(C)-subunit regulates the levels of bioactive activin A by the formation of activin AC heterodimers. To test this hypothesis, we measured activin AC heterodimer production using a novel specific two-site ELISA that we developed for this purpose. In the PC3 human prostate tumor cell line, activin beta(C)-subunit overexpression increased activin AC heterodimer levels, concomitantly reduced activin A levels, and decreased activin signaling. Overall, these data are consistent with a role for the activin beta(C)-subunit as a regulatory mechanism to reduce activin A secretion via intracellular heterodimerization.